



**NDA 50-779/S-001**

B. Braun Medical Inc.  
Attention: John G. D'Angelo, M.S., R.Ph.  
Corporate Vice President, Regulatory and Medical Affairs  
2525 McGaw Avenue  
Irvine, CA 92614-5895

Dear Mr. D'Angelo:

Please refer to your supplemental new drug application dated February 14, 2001, received February 16, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cefazolin for Injection, USP and Dextrose Injection, USP in the DUPLEX™ Container.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the following changes to the label:

*Container Label:*

- 1) The storage temperature information on the container label was changed to read:

“Store at 20-25°C (68-77°F). Excursions to 15-30°C (59-86°F).”

- 2) The date designation following the label part number has been removed to avoid potential confusion with product expiry.

*Package Insert:*

- 3) Throughout the ***Susceptibility Testing*** subsection of the **CLINICAL PHARMACOLOGY** section, “μg” has been changed to “μg”.

- 4) The first paragraph of the **WARNINGS** section has been revised to read:

“BEFORE THERAPY WITH CEFAZOLIN FOR INJECTION USP AND DEXTROSE INJECTION USP IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFAZOLIN, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS DRUG PRODUCT IS GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC

REACTION TO CEFZOLIN FOR INJECTION USP AND DEXTROSE INJECTION USP OCCURS, DISCONTINUE TREATMENT WITH THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTIHISTAMINES, CORTICOSTEROIDS, PRESSOR AMINES AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.”

- 5) The second sentence of the **WARNINGS** section has been revised to read:

“Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of ‘antibiotic-associated colitis’.”

- 6) The third sentence of the fourth paragraph of the **WARNINGS** section has been revised to read:

“In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an oral antibacterial drug clinically effective against *C. difficile* colitis.”

- 7) The **Pediatric Use** subsection of the **PRECAUTIONS** section has been revised to read:

“The potential for toxic effects in pediatric patients from chemicals that may leach from the single-dose IV preparation in plastic has not been determined.”

- 8) In the **DUPLEX™ Drug Delivery System Directions for Use** subsection, the first step under **Removal from Multi-Pack Tray** has been revised to read:

“Tear tape strips from one or both sides of the tray. Remove top tray.”

- 9) In the **DUPLEX™ Drug Delivery System Directions for Use** subsection, the second subheader was retitled “**Patient labeling and Drug Powder/Diluent Inspection**” and the sixth bullet (“Apply patient-specific label on foil side of container. USE CARE to avoid activation.”) under this subheader was moved to the first position.

- 10) In the **HOW SUPPLIED** section, the storage information was revised to read:

“Store the unactivated unit at 20-25°C (68-77°F). Excursions permitted to 15-30°C (59-86°F).”

- 11) In the **HOW SUPPLIED** section, the issue date was changed from April 2000 to January 2001.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted February 14, 2001, immediate container and carton labels submitted February 14, 2001). Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care

Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Beth Duvall-Miller, Regulatory Health Project Manager, at (301) 827-2125.

Sincerely,

*{See appended electronic signature page}*

Janice M. Soreth, M.D.  
Acting Director  
Division of Anti-Infective Drug Products  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research